REMARKS

Applicant's wish to thank the Examiner for the courtesy extended in interviewing this matter on January 30, 2004. Claims 63-92 remain pending in this application. Claims 77, 78, 82, 83, 84 and 89 have been amended pursuant to Examiner's suggestions at the personal interview held on January 30, 2004. Said claims should now be allowable given the removal of "or (ii) TSH receptor fragment". Applicant's reserve the right to pursue claims including this language at a later time. Claim 91 and 92 were added herein. Applicant respectfully asserts that the addition of claims 91 and 92 does not add new matter. Favorable reconsideration is respectfully requested in light of the remarks submitted herein.

Claims 77-90 remain rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Applicant respectfully traverses this rejection.

Applicant has reviewed the Examiner's rejection, and respectfully disagrees with the Examiner's understanding of the invention.

The invention includes:

A kit for use in screening a sample of body fluid for autoantibodies to a thyroid stimulating hormone (TSH) receptor, which kit comprises:

(a) a source of a TSH receptor having at least first and second distinct epitope regions, wherein autoantibodies to said TSH receptor bind to said first epitope region but not said second epitope region;

(b) at least one antibody that binds to said second epitope region;

(c) means for contacting said TSH receptor with at least said sample of body fluid being screened and said antibody of (b), whereby said contacting means allow:

autoantibodies when present in said sample of body fluid being screened to bind to said first epitope region of said TSH receptor; and

said antibody of (b) to bind to said second epitope region of said TSH receptor; and

(d) means for monitoring binding of said autoantibodies provide an indication of the presence of autoantibodies to said TSH receptor in said sample of body fluid being screened.

Therefore, to enable this invention, the specification, in combination with the skill of one of ordinary skill in the art, must teach one of ordinary skill in the art how to make and use the

invention. One component of the invention includes "a source of a TSH receptor, said TSH receptor having at least first and second distinct epitope regions, wherein autoantibodies to said TSH receptor bind to said first epitope region but not said second epitope region".

The specification provides explicit guidance on how to prepare recombinant TSHR preparations. Example 2, as stated by the Examiner (page 5 of August 12, 2003 office action), describes the preparation of a stable cell line for expressing the TSH receptor. Therefore, Example 2 must provide enablement for element (a) of claim 77.

Element (b) of claim 77 now recites "at least one antibody , or fragment thereof, that binds to said second epitope region of said TSH receptor of (a)". Applicant also asserts that the specification provides explicit guidance on how to make this portion of the invention. Example 4 creates a fusion protein from the 3' end of cDNA of TSHR with glutathione S-transferase. Example 5 uses this fusion protein to make monoclonal antibodies. These monoclonal antibodies made in Example 5, are one example of "at least one antibody, or fragment thereof, that binds to said second epitope region of said TSH receptor".

But not Mab that binds to 2nd epitope region

The previously submitted declaration noted that this region was used because it represents a region of the TSH receptor that is almost entirely intracellular. It is desirable to create the monoclonal antibody, i.e., "the antibody, or fragment thereof, that binds to said second epitope region of said TSH receptor" from this region because it ensures that the second epitope region on the TSH receptor will not overlap the first epitope region. This is the case because the first epitope region of the TSH receptor is the region where autoantibodies (i.e., antibodies already within a patient for example) bind to the TSH receptor and this binding of autoantibodies takes place on the outside of the cell. Therefore, utilizing an intracellular region of the TSH receptor allows creation of a monoclonal antibody that will not interfere or overlap with the normal binding of the autoantibodies that are to be monitored.

The Examiner notes at numerous points in the office action that the specification fails to teach two specific epitope regions on the TSH receptor. Applicant respectfully asserts that such teaching is not necessary because the specification does teach how to make and use the invention without including this information. The specific regions on the TSH receptor that are bound to the antibodies are irrelevant. The only important aspect of the two sites is that they do not overlap. Creation of the monoclonal antibody (i.e., element (b) of claim 77) for binding to the second epitope, by using an intracellular region of the TSH receptor ensures that there will be no

Fails to recite this part aspect in claims

overlap because the autoantibody, which binds to the first epitope, binds to an extracelluar portion of the TSH receptor.

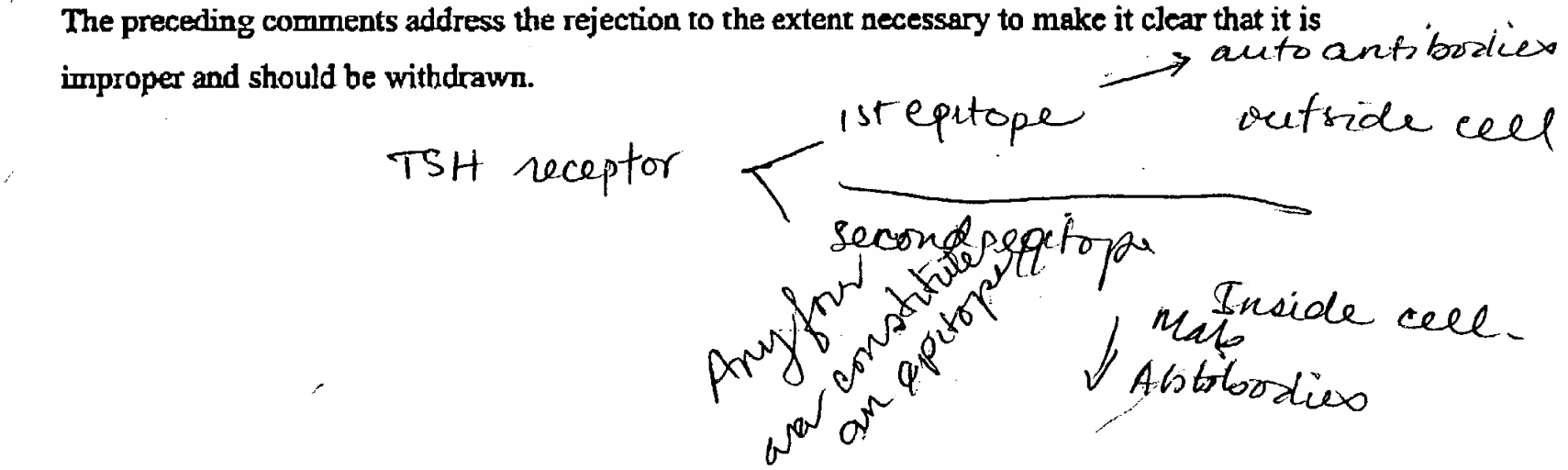
In specific address to the fourth paragraph on page 4 of the office action, Applicant offers the following. The Examiner quotes the declaration filed on May 19, 2003: "example 4 teaches that the last 60 amino acids of the TSHR encoded by cDNA base pairs 1809-2295 was employed in the fusion protein because it represents a region of the TSHR that is almost entirely intracellular and as such is unlikely to interact with the TSHR autoantibodies." The Examiner then asserts that "[s]uch fact is contrary to the requirement of claim 77 part (a) that that TSHR fragment has epitopes that are recognized by the autoantibodies. Therefore, the generated monoclonal antibodies would not bind to the same epitopes as the autoantibodies as required in the claims of the present invention."

Applicant respectfully asserts the Examiner has misunderstood the import of Example 4. The purpose of Example 4 was to make the "at least one antibody, or fragment thereof, that binds to said second epitope region of said TSH receptor". The TSH receptor referred to in clause (b) is that of clause (a), i.e. the TSH receptor that has a first and second epitope region. The fragment utilized in Example 4 was utilized because it does not include the first epitope region. Such a fragment allows for the creation of an antibody that cannot possibly bind the first epitope region.

This specific region must be in claim 77

In such a manner, the specification teaches element (a), a TSH receptor with a first epitope region (for binding to autoantibodies) and a second epitope region (for binding to the antibody of element (b); and element (b) the at least one antibody that binds to the second epitope region, without specifically identifying the two epitope regions.

Applicant does not necessarily agree with the Examiner's treatment of the Wands factor. The preceding comments address the rejection to the extent necessary to make it clear that it is improper and should be withdrawn.



Conclusion

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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